This Page Is Inserted by IFW Operations and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents will not correct images, please do not report the images to the Image Problem Mailbox.



PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

- (51) International Patent Classification ⁶:
 C07C 275/28, C07D 213/75, 257/04,
 231/12, 401/12, A61K 31/17, 31/44,
 31/41, C07D 213/40, 307/38, 277/28,
 233/54, C07C 311/21, C07D 333/20
- (11) Int
- (11) International Publication Number:

WO 96/10559

(43) International Publication Date:

11 April 1996 (11.04.96)

(21) International Application Number:

PCT/JP95/01982

A1

(22) International Filing Date:

29 September 1995 (29.09.95)

(30) Priority Data:

9419970.0 4 October 1994 (04.10.94) GB 9506720.3 31 March 1995 (31.03.95) GB 9514021.6 10 July 1995 (10.07.95) GB

- Osaka 532 (JP).
 - (81) Designated States: AU. CA, CN, HU, JP, KR, MX, RU, US, European patent (AT, BE, CH, DE, DK, ES, FR, OB, GR, IE, IT, LU, MC, NL, PT, SE).

(74) Agent: SEKI, Hideo; Fujisawa Pharmacentical Co., Ltd., Osaka

Factory, 1-6, Kashima 2-chome, Yodogawa-ku, Osaki-shi,

- (71) Applicant (for all designated States except US): FUIISAWA PHARMACEUTICAL CO., LTD. [JP/JP]; 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541 (JP).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): TERASAWA, Takeshi [JP/JP]; 1625-302, Matsugaokanakamachi, Kawachinaganoshi, Osaka 586 (JP). TANAKA, Akira [JP/JP]; 9-10-302, Nakano-cho, Takarazuka-shi, Hyogo 665 (JP). CHIBA, Toshiyuki [JP/JP]; 1-1-503, Nakatsuji-cho, Nara-shi, Nara 630 (JP). TAKASUGI, Hisashi [JP/JP]; 3-116-10, Mozu Umekita, Sakai-shi, Osaka 591 (JP).

Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: UREA DERIVATIVES AND THEIR USE AS ACAT-INHIBITORS

(57) Abstract

Urea derivatives of formula (I), wherein R¹ is a group of formula (I) (in which R⁴ is aryl which may have suitable substituent(s), or heterocyclic group which may have suitable substituent(s), and Y is bond, lower alkylene, -S-, -O-, (a), -CH-, -CONH-, (b), (in which R⁷ is lower alkyl), -NHSO₂-, -SO₂NH-, -SO₂NHCO- or -CONHSO₂-); or thiazolyl, imidazolyl, pyrazolyl, pyridyl,

$$R^{1}-(CH_{2})_{n}-N-C-NH-R^{3}$$
 (I)

imidazolyl, pyrazolyl, pyridyl, thienyl, furyl, isoxazolyl or chromanyl, each of which may have suitable substituent(s); R² is lower alkyl, lower alkoxy(lower)alkyl, cycloalkyl, ar(lower)alkyl which may have suitable substituent(s), heterocyclic group or heterocyclic(lower)alkyl, R³ is aryl which may have suitable substituent(s) or heterocyclic group which may have suitable substituent(s), and n is 0 or 1, and a pharmaceutically acceptable salt thereof which are useful as a medicament in the treatment of hypercholesterolemia, hyperlipidemia and atherosclerosis.

- 210 -

CLAIMS

-11-11-10-120pt & 1377/14/17/0

1. A compound of the formula :

$$R^{1}-(CH_{2})_{\pi}-N-C-NH-R^{3}$$

Wherein

 \mathbb{R}^1 is a group of the formula :

(in which

R⁴ is aryl which may have suitable substituent(s), or heterocyclic group which may have suitable substituent(s), and

Y is bond, lower alkylene, -S-, -O-, -C-, =CH-, -CONH-, -N-CO-, (in which R⁷ is lower R⁷ alkyl), -NHSO₂-, -SO₂NH-, -SO₂NHCO- or -CONHSO₂-); cr

thiazolyl, imidazolyl, pyrazolyl, pyridyl, thienyl, furyl, isoxazolyl or chromanyl, each of which may have suitable substituent(s);

R² is lower alkyl, lower alkoxy(lower)alkyl, cycloalkyl, ar(lower)alkyl which may have suitable substituent(s), heterocyclic group or heterocyclic(lower)alkyl,

R³ is aryl which may have suitable substituent(s) or heterocyclic group which may have suitable WO 96/10559

PCT/JP95/01982

- 211 -

substituent(s), and
n is 0 or 1,
and a pharmaceutically acceptable salt thereof.

5 2. A compound of claim 1, wherein R^1 is a group of the formula :

10.

15

20

25

35

(in which

R⁴ is phenyl which may have 1 to 3 substituent(s) selected from the group consisting of halogen, lower alkyl, di(lower)alkylamino, protected amino, cyano, heterocyclic group which may have mono(or di or tri)—ar(lower)alkyl, hydroxy, protected hydroxy and mono(or di or tri)halo(lower)alkyl; or thienyl, pyrazolyl, imidazolyl, triazolyl, pyridyl, pyrrolyl, tetrazolyl, oxazolyl, thiazolyl, oxadiazolyl, piperazinyl, thiazolidinyl or methylenedioxyphenyl, each of which may have 1 to 3 substituent(s) selected from the group consisting of lower alkyl, mono(or di or tri)ar(lower)alkyl and oxo;

thiazolyl, imidazolyl, pyrazolyl, pyridyl,